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Claims

A process for preparing a compound of the formula:

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A is selected from CH₂ and NR;

B, D and E are independently selected from CH and N;

Y is

wherein:

- (a) phenyl, optionally substituted with 1-3 substituents independently selected from R⁴;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from R⁴;
- (c) C₃-C₈ cycloalkyl, optionally substituted with 1-2 substituents independently selected from R⁴;
- (d) C₃-C₈ cycloalkynyl, optionally substituted with 1-2 substituents independently selected from R⁴;
- (e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR²- and -S(O)_n-, optionally substituted with 1-3 substituents independently selected from R⁴;
- (f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR²- and -S(O)_n- optionally substituted with 1-3 substituents independently selected from R⁴; or
- (g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of -O-, -NR²-, NR²- and -S(O)_n-, optionally

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substituted with 1-3 substituents independently selected from R⁴;

 Z^1 is

- (a) $-(CH_2)_p W(CH_2)_{q}$;
- (b) -O(CH₂)_p CR⁵R⁶-;
- (c) $-O(CH_2)_pW(CH_2)_o$;
- (d) -OCHR²CHR³-; or
- (e) -SCHR²CHR³-;

G is

10 (a) $-NR^7R^8$;

(b)

$$-N$$
 $(CH_2)_m$ Z^2

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wherein n is 0, 1 or 2; m is 1, 2 or 3; Z² is -NH-, -O-, -S-, or -CH₂-; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R⁴; or

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a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R⁴;

25 Z¹ and G in combination may be

$$-0CH_2 \longrightarrow \stackrel{R^2}{\longrightarrow} n$$

30 W is

- (a) -CH₂-;
- (b) -CH=CH-;
- (c) -O-;
- (d) $-NR^2$ -;

C₁-C₄ alkylamino;

(p)

C₁-C₄ dialkylamino; -NHSO₂R; -NO₂; (s) (t) -aryl; or -OH. (u) 5 R⁵ and R⁶ are independently C₁-C₈ alkyl or together form a C₃-C₁₀ carbocyclic ring; R7 and R8 are independently (a) phenyl; a C₃-C₁₀ carbocyclic ring, saturated or unsaturated; 10 (b) a C₃-C₁₀ heterocyclic ring containing up to two heteroatoms, (c) selected from -O-, -N- and -S-; (d) H; C₁-C₆ alkyl; or (e) form a 3 to 8 membered nitrogen containing ring with R⁵ or R⁶; 15 (f) R7 and R8 in either linear or ring form may optionally be substituted with up to three substituents independently selected from C₁-C₆ alkyl, halogen, alkoxy, hydroxy and carboxy; a ring formed by $\ensuremath{\mathsf{R}}^7$ and $\ensuremath{\mathsf{R}}^8$ may be optionally fused to a phenyl ring; e is 0, 1 or 2; 20 m is 1, 2 or 3; n is 0, 1 or 2; p is 0, 1, 2 or 3; q is 0, 1, 2 or 3; and optical and geometric isomers thereof; 25

comprising selectively deacetylating a compound of the formula

wherein R^1 is (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl wherein the alkyl, alkenyl or alkynyl groups are optionally substituted by one to three halo, in the presence of a hydrolytic enzyme and an aqueous buffer solution.

A process according to claim 1, wherein the hydrolytic enzyme is lipase.

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- A process according to claim 1, wherein the hydrolytic enzyme is 3. esterase.
- A process according to claim 1, wherein the hydrolytic enzyme is liver acetone powder. 10
 - 5. A process according to claim 1, wherein the hydrolytic enzyme is lipase from Porcine pancreas, cholesterol esterase from Pseudomonas Fluorscens and cholesterol esterase from Porcine pancreas.
- A process according to claim 2, wherein the lipase is GC-4, PS30, AY30, PGE, AK, N, L-10, AP-12, FAP-15, R-10, G, MAP10, SAM II, lipase from 15 Pseudomonas fluorescens, lipase from Candida cylindracea, Lip-300, lipase from Chromobacterium viscosum, lipase from Mucor miehei, lipase from Pancreatic, lipase from Pseudomonas fluorescens, lipase from Rhizopus niveus, PPL, type II, lipase from Wheat germ, lipase from Rhizopus arrhizus, lipase from Mucor javanicus, lipase from Pseudomonas cepacia, lipase from Cadia lipolytica, lipase from Penicillium roqueforti, lipoprotein lipase ca#70-6571-01, lipase from Porcine pancreas, and lipoprotein lipase ca# 70-1481-01.
 - 7. A process according to claim 3, wherein the esterase is PLE-A, immobilized, hog liver, esterase from Hog pancreas, Porcine liver E-3128, cholesterin-esterase, cholesterol esterase from Pseudomonas fluorescens, cholesterol esterase from Porcine pancreas, cholesterol esterase from Bovine pancreas, cholesterol esterase from Pseudonomas fluorescens, cholesterol esterase

from *Porcine liver*, cholesterol esterase from *Rabbit liver*, cholinesterase, cholinesterase from *Electric eel*, cholinesterase, choloylglycine hydrolase, esterase from *Thermoanaerobium brockii*, esterase from *Bacillus sp* and esterase from *Mucor miehi*.

- 8. A process according to claim 4, wherein the liver acetone powder is cat I-1256, dog I7379, eel I-1266, horse I9627, calf I7876, guinea pig I1631, mouse I8254, goat I2635, chicken I8001, sheep I0132, pigeon I8376, seal I7627, rattlesnake I9885, trout I5131, turtle I-0757, rat I1380, lungfish I7377, salmon I7502, eel (electrophorus electricus) I8380 and lemon shark I1130.
- 9. A process according to claim 1, wherein the hydrolytic enzyme is immobilized on a solid support.

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- 10. A process according to claim 1, wherein the hydrolytic enzyme is a cross-linked enzyme.
- 11. A process according to claim 1, wherein the lipase is in pure crystalline form.
- 12. A process according to claim 1, wherein the aqueous buffer solution is a phosphate, citric acid or boronic acid solution.
- 13. A process according to claim 1, wherein the aqueous buffer solution has a pH between a pH of about 6 to a pH of about 8.
 - 14. A process according to claim 1, for preparing a compound of the formula

comprising selectively deacetylating a compound of the formula

VIII

wherein R^1 is (C_1-C_6) alkyl, (C_2-C_6) alkynyl, (C_2-C_6) alkenyl wherein the alkyl, alkenyl or alkynyl groups are optionally substituted by one to three halo in the presence of a hydrolytic enzyme and an aqueous buffer solution.

15. A process for preparing a compound of the formula:

15 wherein:

A is selected from CH₂ and NR;

B, D and E are independently selected from CH and N;

Y is

- (a) phenyl, optionally substituted with 1-3 substituents independently selected from R⁴;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from R⁴;
- (c) C₃-C₈ cycloalkyl, optionally substituted with 1-2 substituents independently selected from R⁴;

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		(d)"	C ₃ -C ₈ cycloalkynyl, optionally substituted with 1-2 substituents				
	·		independently selected from R4;				
	•	(e)	a five membered heterocycle containing up to two				
			heteroatoms selected from the group consisting of -O-, -NR ² -				
5	•		and -S(O) _n -, optionally substituted with 1-3 substituents				
-		•	independently selected from R4;				
	*	(f)	a six membered heterocycle containing up to two heteroatoms				
			selected from the group consisting of -O-, -NR 2 - and -S(O) $_n$ -				
			optionally substituted with 1-3 substituents independently				
.10			selected from R ⁴ ; or				
		(g)	a bicyclic ring system consisting of a five or six membered				
		•	heterocyclic ring fused to a phenyl ring, said heterocyclic ring				
: .			containing up to two heteroatoms selected from the group				
			consisting of -O-, -NR ² -, NR ² - and -S(O) _n -, optionally				
15			substituted with 1-3 substituents independently selected from				
			R⁴;				
	Z ¹ is						
		(a)	-(CH2)p W(CH2)q-,				
		(b)	-O(CH₂) _p CR⁵R⁶-;				
20		(c)	-O(CH ₂) _p W(CH ₂) _q ;				
		(d)	-OCHR ² CHR ³ -; or				
		(e)	-SCHR ² CHR ³ -;				
	G is		7-9				
		(a)	-NR ⁷ R ⁸ ;				
25		(b)					
			/(CH ₂) _m —				
			$-N$ $(CH_2)_m$ Z^2				
	· .		(CH ₂)n/				

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wherein n is 0, 1 or 2; m is 1, 2 or 3; Z^2 is -NH-, -O-, -S-, or

carbon with one to three substituents and, optionally,

-CH₂-; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on

independently on nitrogen with a chemically suitable substituent selected from R⁴; or

 (c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R⁴;

Z¹ and G in combination may be

$$-0CH_2 \longrightarrow \stackrel{R^2}{\searrow} n$$

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W is

- (a) -CH₂-;
- (b) -CH=CH-;
- (c) -O-;
- (d) $-NR^2$ -;
- (e) $-S(O)_n$ -;
- **(f)**

-C-

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- (g) -CR²(OH)-;
- (h) -CONR²-;
- (i) -NR²CO-;
- (j)

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(k) -C≡C-;

R is hydrogen or C_1 - C_6 alkyl;

R² and R³ are independently

- (a) hydrogen; or
- (b) C₁-C₄ alkyl;

R⁴ is

(a) hydrogen;

			(b)	halogen;					
			(c)	C ₁ -C ₆ alkyl;		• . •			
		•	(d)	C₁-C₄ alkoxy;			4	,	
•			(e)	C ₁ -C ₄ acyloxy;		,			
5			(f)	C₁-C₄ alkylthio;		•			
			(g)	C ₁ -C ₄ alkylsulfinyl;					
			(h)	C ₁ -C ₄ alkylsulfonyl;	·.				
			(i)	hydroxy (C ₁ -C ₄)alkyl	l;				
•			(j)	aryl (C₁-C₄)alkyl;				•	
10	٠.		(k)	-CO₂H;				•	
		.'	(I)	-CN;					
			(m)	-CONHOR;					
			(n)	-SO₂NHR;					
			(o)	-NH ₂ ,				•	٠
15	•	•	(p)	C ₁ -C ₄ alkylamino;	•				
			(q)	C ₁ -C ₄ dialkylamino;	•			•	1
			(r)	-NHSO₂R,					•
			(s)	-NO ₂ ;					•
			(t)	-aryl; or					
20			(u)	-OH.					
		R⁵ and	l R⁵ are	independently C ₁ -C ₈	alkyl or t	togethe	r form a	C ₃ -C ₁₀ cart	oocyclic
	ring;					•	•		
		R ⁷ and		independently				· · · .	
	· .:		(a)	phenyl;					
25 _.			(b)	a C ₃ -C ₁₀ carbocyclic					
			(c)	a C ₃ -C ₁₀ heterocyclic			up to tv	vo heteroato	oms,
				selected from -O-, -N	N- and -S	S-;	•	•	
			(d) _.	H;	٠			•	
	•		(e) ·	C ₁ -C ₆ alkyl; or					
30			(f)	form a 3 to 8 members					
		R ⁷ and	IR ⁸ in e	ither linear or ring for	rm may o	optional	ly be su	bstituted wi	th up to
	three substituents independently selected from C ₁ -C ₆ alkyl, halogen, alkoxy, hydroxy								

a ring formed by R⁷ and R⁸ may be optionally fused to a phenyl ring;

and carboxy;

e is 0, 1 or 2;

m iš 1, 2 or 3;

n is 0, 1 or 2;

p is 0, 1, 2 or 3;

q is 0, 1, 2 or 3;

and optical and geometric isomers thereof;

comprising enzymatically resolving of a compound of the formula

wherein R¹ is (C₁-C₆)alkyl, (C₂-C₆)alkenyl, (C₂-C₆)alkynyl wherein the alkyl, alkenyl or alkynyl groups are optionally substituted by one to three halo in the presence of a lipase and an aqueous buffer solution; and (b) reacting the compound of formula IV so formed

wherein R¹ is as defined above, with a base in the presence of a polar protic solvent.

- 16. A process according to claim 15, wherein the aqueous buffer solution is a phosphate, citric acid or boronic acid solution.
 - 17. A process according to claim 15, wherein the lipase from Mucor miehei.
- 18. A process according to claim 15, wherein the base is sodium methoxy, sodium hydroxide, lithium hydroxide or potassium hydroxide.
- 19. A process according to claim 15, wherein the polar protic solvent is methanol, ethanol or water.

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- 20. A process according to claim 15, wherein the lipase is immobilized on a solid support.
- 21. A process according to claim 15, wherein the lipase is a cross-linked enzyme.
- 22. A process according to claim 15, wherein the lipase is in pure crystalline form.
 - 23. A process according to claim 15, for preparing a compound of the formula

comprising enzymatically resolving of a compound of the formula

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VIII

wherein R^1 is (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl wherein the alkyl, alkenyl or alkynyl groups are optionally substituted by one to three halo in the presence of a lipase and an aqueous buffer solution; and (b) reacting the compound of Formula X so formed

wherein R¹is as defined above, with a base in the presence of a polar protic solvent.

24. A process for preparing a compound of the formula:

wherein:

A is selected from CH₂ and NR;

B, D and E are independently selected from CH and N;

5 Y. is

(a) phenyl, optionally substituted with 1-3 substituents independently selected from R⁴;

(b) naphthyl, optionally substituted with 1-3 substituents independently selected from R⁴;

(c) C₃-C₈ cycloalkyl, optionally substituted with 1-2 substituents independently selected from R⁴;

(d) C₃-C₈ cycloalkynyl, optionally substituted with 1-2 substituents independently selected from R⁴;

(e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR²- and -S(O)_n-, optionally substituted with 1-3 substituents independently selected from R⁴;

(f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -NR²- and -S(O)_n- optionally substituted with 1-3 substituents independently selected from R⁴; or

(g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of -O-, -NR²-, NR²- and -S(O)_n-, optionally substituted with 1-3 substituents independently selected from R⁴;

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 Z^1 is

- (a) $-(CH_2)_p W(CH_2)_{q}$;
- (b) $-O(CH_2)_p CR^5R^6$ -;
- (c) $-O(CH_2)_pW(CH_2)_q$;
- (d) -OCHR²CHR³-; or '
- (e) -SCHR²CHR³-;

G is

(a) $-NR^7R^8$;

(b)

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$$-N$$
 $(CH_2)_m$ Z^2

wherein n is 0, 1 or 2; m is 1, 2 or 3; Z² is -NH-, -O-, -S-, or -CH₂-; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R⁴; or

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(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R⁴;

Z¹ and G in combination may be

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$$-0CH_2 \longrightarrow \stackrel{R^2}{\longrightarrow} n$$
;

W is

- (a) -CH₂-;
- (b) -CH=CH-;
- (c) -O-;
- (d) $-NR^2$ -;
- (e) $-S(O)_n$ -;
- **(f)**

(h) -CONR²-;

(i) -NR²CO-;

(j)

$$\left\langle S\right\rangle -$$
 ; or

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R is hydrogen or C₁-C₆ alkyl;

R² and R³ are independently

- (a) hydrogen; or
- (b) C_1 - C_4 alkyl;

R⁴ is

- (a) hydrogen;
- (b) halogen;
- (c) C₁-C₆ alkyl;
- (d) C_1 - C_4 alkoxy;
- (e) C₁-C₄ acyloxy;
- (f) C_1 - C_4 alkylthio;
- (g) C₁-C₄ alkylsulfinyl;
- (h) C₁-C₄ alkylsulfonyl;
- (i) hydroxy (C_1-C_4) alkyl;
- (j) aryl (C₁-C₄)alkyl;
- (k) $-CO_2H$;
- (I) -CN;
- (m) -CONHOR;
- (n) -SO₂NHR;
- (o) -NH₂;
- (p) C₁-C₄ alkylamino;
- (q) C₁-C₄ dialkylamino;
- (r) -NHSO₂R;

- (s) -NO₂,
- (t) -aryl; or
- (u) -OH.

R⁵ and R⁶ are independently C₁-C₈ alkyl or together form a C₃-C₁₀ carbocyclic

5 ring;

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R⁷ and R⁸ are independently

- (a) phenyl;
- (b) a C₃-C₁₀ carbocyclic ring, saturated or unsaturated;
- (c) a C₃-C₁₀ heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;
- (d) H;
- (e) C_1 - C_6 alkyl; or
- (f) form a 3 to 8 membered nitrogen containing ring with R⁵ or R⁶;

R⁷ and R⁸ in either linear or ring form may optionally be substituted with up to three substituents independently selected from C₁-C₆ alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by R7 and R8 may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

20 n is 0, 1 or 2;

p is 0, 1, 2 or 3;

q is 0, 1, 2 or 3;

and optical and geometric isomers thereof;

comprising enzymatically resolving of a compound of the formula

in the presence of a lipase and an acetylating agent, and (b) reacting the compound of formula IV so formed

wherein R^1 is (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl wherein the alkyl, alkenyl or alkynyl groups are optionally substituted by one to three halo, with a base in the presence of a polar protic solvent.

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- 25. A process according to claim 24, wherein the hydrolytic enzyme is a lipase.
- 26. A process according to claim 24, wherein the lipase is GC-4, PS30, AY30, PGE, AK, N, L-10, AP-12, FAP-15, R-10, G, MAP10, SAM II, lipase from Pseudomonas fluorescens, lipase from Candida cylindracea, Lip-300, lipase from Chromobacterium viscosum, lipase from Mucor miehei, lipase from Pancreatic, lipase from Pseudomonas fluorescens, lipase from Rhizopus niveus, PPL, type II, lipase from Wheat germ, lipase from Rhizopus arrhizus, lipase from Mucor javanicus, lipase from Pseudomonas cepacia, lipase from Cadia lipolytica, lipase from Penicillium roqueforti, lipoprotein lipase ca#70-6571-01, lipase from Porcine pancreas, and lipoprotein lipase ca#70-1481-01.
- 27. A process according to claim 24, wherein the acetylating agent is ethyl acetate, vinyl acetate, chloroacetate or trifluoroacetate.
- 28. A process according to claim 24, wherein the base is sodium methoxy, sodium hydroxide, lithium hydroxide or potassium hydroxide.
- 29. A process according to claim 24, wherein the polar protic solvent is methanol, ethanol or water.
- 30. A process according to claim 24, wherein the lipase is immobilized on asolid support.

- 31. A process according to claim 24, wherein the lipase is a cross-linked enzyme.
- 32. A process according to claim 24, wherein the lipase is in pure crystalline form.
 - 33. A process according to claim 24, for preparing a compound of the formula

comprising enzymatically resolving of a compound of the formula

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in the presence of a lipase and acetylating agent, and (b) reacting the compound of Formula X so formed

XII

wherein R^1 is (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl wherein the alkyl, alkenyl or alkynyl groups are optionally substituted by one to three halo, with a base in the presence of a polar protic solvent.

34. A process for preparing a compound of the formula:

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15 wherein:

A is selected from CH₂ and NR;

B, D and E are independently selected from CH and N;

Y is

- (a) phenyl, optionally substituted with 1-3 substituents independently selected from R⁴;
- (b) naphthyl, optionally substituted with 1-3 substituents independently selected from R⁴;
- (c) C₃-C₈ cycloalkyl, optionally substituted with 1-2 substituents independently selected from R⁴;

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(d) C₃-C₈ cycloalkynyl, optionally substituted with 1-2 substituents independently selected from R⁴;

	(e) "	a five membered heterocycle containing up to two
		heteroatoms selected from the group consisting of -O-, -NR ² -
	*	and $-S(O)_{n-}$, optionally substituted with 1-3 substituents
•		independently selected from R ⁴ ;
5	(f)	a six membered heterocycle containing up to two heteroatoms
41		selected from the group consisting of -O-, -NR 2 - and -S(O) $_n$ -
	•	optionally substituted with 1-3 substituents independently
		selected from R ⁴ ; or
	(g)	a bicyclic ring system consisting of a five or six membered
10		heterocyclic ring fused to a phenyl ring, said heterocyclic ring
		containing up to two heteroatoms selected from the group
		consisting of -O-, -NR ² -, NR ² - and -S(O) _n -, optionally
		substituted with 1-3 substituents independently selected from
•		R⁴;
15 Z ¹		
•••	(a)	$-(CH_2)_p W(CH_2)_q$ -;
	(b)	-O(CH ₂) _p CR ⁵ R ⁶ -;
N	(c)	-O(CH2)pW(CH2)q;
	(d)	-OCHR ² CHR ³ -; or
20	(e)	-SCHR ² CHR ³ -;
Gi		-NR ⁷ R ⁸ ;
•	(a) (b)	*NIX IX ,
	(b)	
		$(CH_2)_m$

25,

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wherein n is 0, 1 or 2; m is 1, 2 or 3; Z² is -NH-, -O-, -S-, or -CH₂-; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from R⁴; or

(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from R⁴;

Z¹ and G in combination may be

5

$$-OCH_2 \longrightarrow \bigwedge^{R^2} n$$

W is

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- (a) -CH₂-;
- (b) -CH=CH-;
- (c) -O-;
- (d) $-NR^2$ -;
- (e) $-S(O)_{n}$ -;

15 .

(f)

- (g) -CR²(OH)-;
 - (h) -CONR²-;
 - (i) -NR²CO-;
 - (j)

_________; or

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R is hydrogen or C₁-C₆ alkyl; R² and R³ are independently

- (a) hydrogen; or
- (b) C₁-C₄ alkyl;

R⁴ is

- (a) hydrogen;
- (b) halogen;
- (c) C_1 - C_6 alkyl;

```
C<sub>1</sub>-C<sub>4</sub> alkoxy;
                                               C<sub>1</sub>-C<sub>4</sub> acyloxy;
                                    (e)
                                   (f)
                                               C<sub>1</sub>-C<sub>4</sub> alkylthio;
                                   (g)
                                               C<sub>1</sub>-C<sub>4</sub> alkylsulfinyl;
                                   (h)
                                               C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl;
                                   (i)
                                               hydroxy (C<sub>1</sub>-'C<sub>4</sub>)alkyl;
                                   (j)
                                              aryl (C<sub>1</sub>-C<sub>4</sub>)alkyl;
                                   (k)
                                              -CO<sub>2</sub>H;
                                   (1)
                                              -CN;
  10
                                   (m)
                                              -CONHOR;
                                              -SO<sub>2</sub>NHR;
                                  (n)
                                              -NH<sub>2</sub>;
                                  (o)
                                  (p)
                                              C<sub>1</sub>-C<sub>4</sub> alkylamino;
                                             C<sub>1</sub>-C<sub>4</sub> dialkylamino;
                                  (p)
  15
                                             -NHSO2R;
                                  (r)
                                  (s)
                                             -NO<sub>2</sub>;
                                  (t)
                                             -aryl; or
                                 (u)
                                             -OH.
                      \mathsf{R}^5 and \mathsf{R}^6 are independently \mathsf{C}_1\text{-}\mathsf{C}_8 alkyl or together form a \mathsf{C}_3\text{-}\mathsf{C}_{10} carbocyclic
 20
          ring;
                     R7 and R8 are independently
                                 (a)
                                            phenyl;
                                            a C<sub>3</sub>-C<sub>10</sub> carbocyclic ring, saturated or unsaturated;
                                 (b)
                                            a C<sub>3</sub>-C<sub>10</sub> heterocyclic ring containing up to two heteroatoms,
                                (c)
25
                                            selected from -O-, -N- and -S-;
                                (d)
                                            H;
                                (e)
                                            C<sub>1</sub>-C<sub>6</sub> alkyl; or
                                           form a 3 to 8 membered nitrogen containing ring with R<sup>5</sup> or R<sup>6</sup>;
                                (f)
                    R<sup>7</sup> and R<sup>8</sup> in either linear or ring form may optionally be substituted with up to
         three substituents independently selected from C<sub>1</sub>-C<sub>6</sub> alkyl, halogen, alkoxy, hydroxy
30
         and carboxy;
                    a ring formed by R<sup>7</sup> and R<sup>8</sup> may be optionally fused to a phenyl ring;
```

e is 0, 1 or 2; m is 1, 2 or 3; n is 0, 1 or 2;

p is 0, 1, 2 or 3;

q is 0, 1, 2 or 3;

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and optical and geometric isomers thereof;

comprising enzymatically resolving of a compound of the formula

wherein R1 is (C1-C6)alkyl, in the presence of lipase,

- 35. A process according to claim 34, wherein the lipase is Mucor miehei.
- 36. A process according to claim 34, wherein the lipase is immobilized on a solid support.
- 37. A process according to claim 34, wherein the lipase is a cross-linked enzyme.
- 38. A process according to claim 34, wherein the lipase is in pure crystalline form.
 - 39. A process according to claim 34, wherein the hydrolytic enzyme is lipase from *Porcine pancreas*, cholesterol esterase from Pseudomonas Fluorscens and cholesterol esterase from *Porcine pancreas*.
 - 40. A process according to claim 34, for preparing a compound of the formula

comprising enzymatically resolving of a compound of the formula

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in the presence of lipase.